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OUR COVER

JOSIAH K. LILLY

WE are happy to devote our cover this month to one who is both well known and honored by a legion of men and women the world over and to heartily endorse the decision of the A. Ph. A. committee to bestow upon him the Remington Medal for 1942. This medal, one of the highest awards in pharmacy is presented annually to that man in American Pharmacy who, in the opinion of a distinguished group of leaders, has rendered outstanding service to the cause of pharmacy. In choosing Mr. J. K. Lilly they have indeed made an excellent choice.

Mr. Lilly graduated from the Philadelphia College of Pharmacy in 1892 where he had studied under those stalwarts of early American Pharmacy, Maisch, Sadtler and Remington and one can easily perceive his interest in *real* pharmacy by perusing the thesis submitted as a prerequisite to his graduation.

The contributions which have been made in the interest of American Pharmacy by Mr. Lilly are indeed impressive. The ideals and service rendered in the cause of alleviating human suffering by the organization bearing his name has placed it among the very first in the minds of pharmacists, physicians and the public.

It is doubtful, however, that the full extent of his influence and support in many and diverse directions will ever be completely known and it may truthfully be said that all has been done in a spirit of loyalty and love for both his profession and his fellowman.

EDITORIAL

THE PHARMACY CORPS BILL

PHARMACISTS, generally, are being called upon to actively support H. R. 7432 and S2690 which is intended to increase both the recognition of pharmacy and assist in guaranteeing the same quality of pharmaceutical service in the military that is available for civilians.

The pharmaceutical press is constantly bombarding all pharmacists to contact their congressmen asking that they support this bill and warning that its opposition will be strong and hard to overcome. No one has suggested why this opposition except to hint darkly that powerful influences are pitted against its passage. Actually some very strong arguments have been advanced not against greater recognition of pharmacy but against a separate corps in the army.

We are surely in favor of a greater recognition of real pharmaceutical skill and training by the armed services and there is no question but that the quality of medical service rendered to our boys would be greatly improved from the standpoint of efficiency and safety if this were true. Well-founded reports tell us of men with only a few weeks scanty training given the responsibility of dispensing drugs, a responsibility that in civil life is granted only to men with four years of college training. We know from past experience that this can only lead to serious errors and accidents, a risk to which no one responsible for this situation would care to subject his family or take himself. It is this fact which is the basis for all our pharmacy laws governing civilian practice. Surely with the terrible losses to be expected in battle these avoidable risks can neither be written off as inconsequential nor should those men who will be lost due to faulty pharmaceutical service be classified as expendable. Our men deserve the best that can be given them. All these facts are incontestable. Why then the failure on the part of the armed services to properly recognize pharmacy and its services? The truth is, whether we like it or not, that pharmacy has during the last two decades been degraded in the eyes of both the medical profession and the public by the sandwich counter, the notion department and the cheap

gaudy merchandise of a thousand varieties which are unrelated to the practice of our profession. The corner drug store is still that phase of pharmacy which molds public opinion and public apathy concerning the lack of recognition given us is a perfectly logical result which cannot be corrected by banner waving, speech making and editorials in journals still carrying advertising for questionable merchandise and junk that no *real* pharmacist would sell even on demand.

Fortunately, there is much that is favorable on the balance sheet of pharmacy. Many are the conscientious pharmacists who are doing a splendid job without fanfare but with that quiet and efficient conduct characteristic of professional men The great advances in medicine largely as a result of pharmaceutical research have been a most important factor in making the public duly conscious of the importance of this branch of pharmacy and the ethical manufacturers of drug products have conducted an excellent campaign to make the public more aware of the basic importance of pharmacy as a health profession and its importance in the community life. It is gratifying to learn that our recent graduates in pharmacy are receiving recognition, actual if not official, in both the army and navy since sooner or later their real superiority to the untrained men cannot escape notice. Real recognition is not likely to escape the deserving and like fame it cannot be created simply by a desire to possess it. While we are striving for the passage of a Pharmacy Corps Bill let us ask ourselves why greater recognition has not been ours without the need of such great pressure. If it is passed, let us be thankful; if it is not let us determine to adopt a policy that will place both medical and public opinion behind us rather than on the side-lines. It can be done if we are willing to meet the issue and present Pharmacy in its proper light. We all know where the changes must come. Let us have the necessary determination to see them made.

L. F. Tice.

THE INHIBITORY EFFECT OF LIPOIDS ON DETERGENTS WITH DISINFECTANTS ACTING AGAINST S. AUREUS AND E. TYPHOSA AT DIFFERENT pH VALUES

By Louis Gershenfeld and Maxwell Ibsen

Department of Bacteriology, Philadelphia College of Pharmacy and Science

The synergism and antagonism exhibited between detergents and disinfectants has received considerable attention. Other factors such as pH, etc., exercise a considerable influence and have been discussed in this Journal in several recent papers. This report presents data on the influence of lipoids on this phenomenon

Introduction

THE introduction of synthetic detergents and wetting agents to the broadening fields of application in industry and science has prompted investigators to theorize on the mechanism of their action on membranes and cell surfaces. The development of the theory of monomolecular film balance and the subsequent study of films in a two-dimensional system have done much in furthering an understanding of surface phenomena. In addition, determinations of contact angles after placing a drop of a fluid on a built-up film, demonstrate delicate differences in the surface structure of such films. Sobotka (50) has been able to demonstrate qualitative differences between hydrophobic and hydrophylic substances by this method, and he has shed new light on the significance of organic groupings to surface phenomena.

The role of lipoids and lipoid-like substances in the physiology of the cell has been recognized (17, 52), and their function in the cell membrane in particular has been investigated. Danielli and Harvey (20) have shown that the absorption of a globulin-like protein at the oil surface is probably the basis for the low interfacial tension between the oil and water phases. The lipoid-like nature of the acid-fast group of bacteria is well known and the lipo-protein

structure of the antigenic fraction has been recognized. On the other hand, the action of lipoids on cells has indicated their ability to disrupt and disorganize the membrane structure by their solvent and emulsifying actions. Baker *et al.* (6) present a thorough bibliography on the action of lipoids on cells.

Historical Review

Explanations accounting for the action of synthetic detergents on cells and particularly on bacterial cells are inconclusive, but, consistently indicate the important role of cell lipoids in this action. No one has proven experimentally the action of synthetic detergents on bacteria, but many investigators have advanced theories relating to the surface activity of these substances. Gershenfeld *et al.* (26, 27, 28) have shown the importance of hydrogen-ion concentration and chemical structure to the bactericidal action of the newer type detergents. Baker *et al.* (4, 5) also have indicated the important role of pH in the anti-bacterial properties of wetting agents.

The bactericidal and bacteriostatic actions of synthetic detergents and wetting agents have been recognized and numerous reports have been published regarding their activity. Their direct action on bacteria has been noted (5, 23, 27) and their effects on toxin production by different bacteria (16), on phage, and on viruses (9) have been considered. Baker *et al.* (6) advanced a reasonable hypothesis for the rapid action of detergents on bacterial cells. They concluded that this action was two-fold: "1) Disorganization of cell membrane by virtue of the great surface activity of these compounds, and 2) Denaturation of certain proteins essential to metabolism and growth."

Several workers have shown that certain lipoids decreased the antiseptic action of mercuric chloride, phenol and salvarsan for *Bacillus anthracis.* Their inhibitory action for staphylococcus phage (31) and their detrimental action against lysins and toxins (58) also have been demonstrated. Baker *et al.* (6) noted that germicidal concentrations of detergents were ineffective in the presence of phospholipoids. Studies on the stability of monomolecular films of various fatty acids and long chain alcohols (59) have shown that the introduction of small amounts of detergents beneath the film surface produces a rise in pressure on the film and ultimately causes the rupture of the film. The penetrative power occurred at various speeds de-

pendent on the pH of the medium and furthermore the concentration of fatty acid required to produce this effect also was dependent on the pH.

Purpose

In view of the foregoing presentations concerning the interplay of surface tension, detergent action and lipoid activity in cell membranes, it was considered desirable to determine the effects of the various lipoid-like substances on the activity of synthetic detergents on bacteria.

Experimental

A. *Technique*: In order to simulate as closely as possible the phenomena concerned with surface activity which are met in the practical use of wetting agents on solid surfaces, a technique was developed and employed throughout these experiments. This technique consisted in the use of discs of filter paper, 5.5 mm. in diameter, punched from Whatman No. 2 filter paper by means of an ordinary paper punch, and impregnated with the solutions being investigated. They were allowed to dry completely on a clean glass slide for one-half hour in an incubator at 37.5° C., and then were placed flat on the surface of an inoculated agar plate. The entire procedure was carried out under as aseptic conditions as possible. The paper discs were sterilized before use in the hot air oven, and small tissue forceps kept sterile by heating in an open flame were used to transfer the discs from test solutions to sterile slides for drying and subsequently to agar surfaces. After 18-24 hours of incubation at 37.5° C. the plates were examined and zones of inhibition were accurately measured to 0.2 mm. All measurements were made under identical conditions. It was noted that if a rigid aseptic technique was not followed, the results were not affected, for contaminants were seldom found.

1. *Materials:*

a. Discs—Paper discs of uniform size (5.5 mm. in diameter) were used throughout the study and were punched out of Whatman No. 2 filter paper.

b. Agar—One and one-half per cent. agar medium was used. This was prepared according to specifications of the Food and Drug Administration Technique for Testing Disinfectants by the agar cup

plate method (53). All agar medium prepared was divided into five equal portions and the pH of each portion was adjusted colorimetrically to one of the following pH values: 5, 6, 7, 8, and 9. A check on the Beckman pH meter agreed with the former adjustment to within 0.2 of a pH degree.

c. Test Organisms—The organisms used were a 22-26 hour culture of both a standard F. D. A. strain of *Eberthella typhosa* and a F. D. A. strain of *Staphylococcus aureus,* both incubated and grown in nutrient broth of F. D. A. specifications at 37.5° C. The test cultures were transferred daily in F. D. A. broth and stock cultures were kept on one and one-half per cent. agar slants.

d. Detergents—Accurately prepared 5 per cent. solutions of the various detergents in distilled water were employed as stock solutions. Five grams of the respective detergent were accurately weighed, carefully transferred to a 100 cc. volumetric flask, and made up to the mark with freshly distilled water. Fresh stock solutions were made every month, but fresh working dilutions of these stock solutions were made daily for the experiments. The pH of these solutions varied from 6.2 to 6.6 depending upon the pH of the distilled water. The following table lists the detergents included in the present study.

TABLE I

No.	Product	Composition	Manufacturer
1.	Aerosol OT	Di-octyl sodium sulfosuccinate	Am. Cyanamid and Chemical Corp.
2.	Tergitol 4*	Sodium tetra-decyl sulfate	Carbon and Carbide Co.
3.	Tergitol 4T*	Triethalanolamine tetra-decyl sulfate	Carbon and Carbide Co.
4.	Dupanol C	Technical lauryl sodium sulfate	E. I. DuPont de Nemours and Co.
5.	Nopco SHCO	Sulfonated hydrogenated castor oil	National Oil Products
6.	Triton K 60	Lauryl dimethyl benzyl ammonium chloride	Rohm and Haas
7.	Hydrocide GK	Alkyl hydroxybenzyl dimethyl ammonium phosphate	Rohm and Haas
8.	Product QB	Technical lauryl trimethyl ammonium bromide	E. I. DuPont Co.
9.	DuPont Retarder	Technical stearyl trimethyl ammonium bromide	E. I. DuPont Co.
10.	Nopco CNI-P**		National Oil Products

*Commercial Tergitol 4 and 4T have a 25% active ingredient content.
**Nopco CNI-P contains 20% active cationic material.

e. Lipoids—One per cent. solutions of the lipoid substances in ether were prepared. 250 milligrams of each lipoid-like substance were accurately weighed, transferred to a 25 cc. volumetric flask and made up to the mark with anhydrous ether (U. S. P. XI). Sodium taurocholate and sodium ricinoleate solutions were made with distilled water.

The following table indicates the lipoid-like substances used in this study.

TABLE II

No.	Product	Description	Manufacturer
1.	Oleic acid U. S. P.	Liquid	Merck and Co.
2.	Stearic acid U. S. P.	Powdered	Mallinckrodt Chemical Works
3.	Sodium ricinoleate	Powdered	Sharpe and Dohme
4.	Sodium taurocholate*	Powdered	Merck and Co.
5.	Lecithin	Waxy	Merck and Co.
6.	Cholesterin C. P.	Powdered	Pfanstiehl
7.	Sperm Oil Sterol	Powdered	Difco Mfg. Co.
8.	Cotton Seed Sterol	Powdered	Difco Mfg. Co.

*Contains 45% active material.

A 1 per cent. stock solution of the above lipoids was prepared as described and used throughout the entire experiment. One per cent. aqueous solutions of sodium ricinoleate and taurocholate were found to exert inhibitory effects against *S. aureus* and *E. typhosa* and were, therefore, used in 0.1 per cent. strengths in the following experiments.

2. *Methods:*

In order to assure consistent results it was found advisable to consider the many possible variants entering into the procedure. The relationship between the amount of agar medium and the number of organisms used per plate and the consequent effect of the zones of inhibition were investigated.

The following tables will indicate the relationships noted.

TABLE III

Effect of Varying the Amount of Culture of Bacteria per Plate on the Zone of Inhibition Produced by Hexylresorcinol

S. aureus Culture—cc. per 15 cc. of 1.5% Agar Medium	Hexylresorcinol 1/500	1/1000	1/5000
	Zone of Inhibition in mm.		
.05	1.2	0.5	0
.10	1.2	0.5	0
.20	1.2	0.8	0
.50	1.2	0.5	0
1.00	1.2	0.5	0

TABLE IV

Effect of Varying the Amount of Agar Medium per Plate on the Zone of Inhibition Produced by Hexylresorcinol

Agar Medium 1.5% cc. to 0.1 cc. *S. aureus*	Hexylresorcinol 1/500	1/1000	1/5000
	Zone of Inhibition in mm.		
10.0	2.6	1.0	0
12.0	2.0	1.0	0
15.0	1.5	0.8	0
20.0	1.0	0.5	0
30.0	1.0	0.5	0

It will be noted from the above that the amount of agar medium per plate will influence the zone of inhibition produced by 1/500 and 1/1000 aqueous solutions of hexylresorcinol. For purposes of uniformity it was decided to employ 20 cc. of agar medium and 0.1 cc. of a bacterial suspension of a 22-26 hour broth culture of organisms per plate.

A preliminary test was carried out to determine the effect of 1 per cent. ether solutions of the different lipoids on *S. aureus* and *E. typhosa*. The following table shows the results of these tests.

TABLE V

Inhibition Produced by 1.0% Ether Solutions of Different Lipoids

	Oleic acid	Stearic acid	Lecithin	Cholesterol	Sperm sterol	Cotton sterol	Ether control
	Zone of Inhibition in mm.						
S. aureus	0	0	0	0	0	0	0
E. typhosa	0	0	0	0	0	0	0

TABLE VI

Inhibition Produced by 1.0 and 0.1% Aqueous Solutions of Bile Salts

	Sodium taurocholate (Per cent.)		Sodium ricinoleate (Per cent.)	
	1.0	0.1	1.0	0.1
	Zone of Inhibition in mm.			
S. aureus	1.0	0	1.0	0
E. typhosa	0.8	0	0.5	0

In determining the effect of lipoid-like substances on detergents, disinfectants, and detergent-disinfectant mixtures, the following technique was used. After impregnating the discs with the solutions of detergents, they were allowed to dry for one-half hour in the incubator at 37.5° C. Half of the number of discs were then dipped in the respective lipoid-ether solution while the remaining duplicates were dipped in plain ether and served as control. The discs were completely dry within one minute, after which they were transferred to the surface of previously inoculated agar plates.

Results

The Effect of Anionic and Cationic Detergents on S. aureus and E. typhosa: The effects of five cationic and five anionic detergents in inhibiting the growth of *S. aureus* and *E. typhosa* on agar plates of different pH values is shown in Table VII. The detergents were tested in only one concentration, 1/100, and the figures in the table represent the average of the results obtained in several separate experiments.

It was found that anionic detergents were actively inhibitory against *S. aureus,* showing greatest zones of inhibition on agar of high hydrogen-ion concentration and decreasing with a lowered hydrogen-ion concentration of the agar medium. No zones of inhibition were produced by these detergents against *E. typhosa* at any of the pH values.

The cationic detergents were less active against *S. aureus.* Product QB was the only cationic detergent studied which showed any inhibitory effect against *S. aureus.* This type of surface tension depressant, however, was more active as a group against *E. typhosa.* The anionic detergents showed their maximum inhibitory action on the acid side and the cationic detergents displayed their maximum inhibitory action on the alkaline side. The variations in zones of inhibition of the same concentration of the several detergents at the different pH values are apparent from Table VII.

TABLE VII

Effect of Anionic and Cationic Detergents on S. aureus and E. typhosa at Different pH Values*

pH of Agar	5		6		7		8		9	
Organism	S	T	S	T	S	T	S	T	S	T
Detergents—Aqueous 1:1000	Zone of Inhibition (mm.)									
Aerosol OT	2.2	o	1.6	o	1.0	o	0.5	o	0.5	o
Tergitol 4	0.5	o	0.5	o	+	o	0.5	o	+	o
Tergitol 4T	0.5	o	+	o	+	o	+	o	+	o
Duponol C	3.2	+	3.0	o	2.5	o	2.0	o	1.5	o
Nopco SHCO	+	+	o	o	o	o	o	o	o	o
Triton K 60	o	+	o	+	+	o	+	o	0.5	o
Hydrocide GK	o	+	o	o	o	o	o	o	o	+
Product QB	1.5	o	2.0	o	3.5	+	3.8	+	5.8	+
DuPont Ret. LA	o	o	o	o	o	o	o	o	o	o
Nopco CNI-P	+	+	+	+	+	+	+	+	+	+

*Results represent the average of two experiments.

S = *Staphylococcus aureus.*
T = *Eberthella typhosa.*
o = No visible zone of inhibition.
\+ = Slight zone immediately surrounding edge of disc.

TABLE VIII

Action of Aerosol OT and Product QB on S. aureus and the Effect of Various Lipoids on this Action

pH Agar	5		6		7		8		9	
Detergent (Aqueous)— 1:100	OT	QB	OT	QB	OT	QB	OT	QB	OT	QB
Lipoid (Ether)— 1:1000	Zone of Inhibition (mm.)									
Oleic acid	1.7	—	0.8	—	0.5	—	0.5	—	—	—
Stearic acid	1.8	—	1.0	0.9	0.5	1.9	0.5	2.6	0.7	3.7
Na ricinoleate*	2.3	1.4	0.9	2.2	0.5	3.0	—	3.5	0.8	4.3
Na taurocholate*	1.8	1.5	1.4	2.2	—	2.9	0.5	3.8	0.5	4.9
Cholesterin	2.7	0.5	1.0	1.1	1.0	1.7	0.5	2.5	0.5	4.2
Lecithin	1.1	—	—	0.5	—	1.2	0.5	1.8	0.5	2.4
Sperm Sterol	1.5	0.5	0.8	1.2	0.5	2.1	0.5	2.4	0.6	4.4
Cotton Sterol	1.5	—	0.9	1.2	0.6	2.0	0.5	3.1	0.5	4.5
Controls										
Det. Aq. 1:100	3.8	1.0	2.7	2.1	2.1	3.5	1.8	4.8	1.5	5.5
Ether	o	o	o	o	o	o	o	o	o	o

*Sodium ricinoleate and taurocholate were used in 0.1% aqueous concentrations.

TABLE IX

The Effect of Aerosol OT and Product QB on the Inhibition of Metaphen for S. aureus and E. typhosa at Different pH Values†*

pH of Agar	5		6		7		8		9	
Organism	S	T	S	T	S	T	S	T	S	T
	Zone of Inhibition (mm.)									
Metaphen 1:10,000 (Aq.)	4.0	2.2	3.5	2.5	3.0	2.5	2.0	2.0	1.8	1.6
" and 0.1% QB	3.0	2.6	2.8	2.2	3.0	1.6	1.6	1.2	1.5	1.0
" and 0.1% OT	2.6	2.2	3.0	2.0	3.0	2.0	1.6	1.6	1.5	1.0
Controls										
Alc.—Water**	0	0	0	0	0	0	0	0	0	0
0.1% QB	0	0	0	0	0	0	0	0	0	0
0.1% OT	0	0	0	0	0	0	0	0	0	0

*Metaphen 1:10,000 concentration; made by diluting 1:200 Tincture of Metaphen (Abbott) with distilled water.

**Of same final concentration as used in metaphen dilution.

†Results include average of two separate experiments.

TABLE IXa

The Effect of Lipoids on Inhibition of Metaphen (1:10,000) for S. aureus and E. typhosa at Different pH Values†

pH of Agar	5		6		7		8		9	
Organism	S	T	S	T	S	T	S	T	S	T
	Zone of Inhibition (mm.)									
Metaphen (Aq.) 1:10,000	3.8	5.2	4.0	3.6	4.0	2.4	3.0	1.5	2.0	1.5
" and Stearic acid*	3.0	3.8	3.6	3.0	4.0	2.2	2.8	1.2	1.8	1.5
" and Sodium taurocholate*	3.0	3.4	4.0	2.8	4.0	2.6	2.4	1.2	2.2	1.0
" and Lecithin*	3.5	2.6	3.8	2.8	3.4	2.2	2.6	1.2	2.0	1.2
Controls										
Lipoids	0	0	0	0	0	0	0	0	0	0
Ether	0	0	0	0	0	0	0	0	0	0

*Lipoids made up in 1.0% concentration with anhydrous ether.

†Results include average of two separate experiments.

TABLE X

The Effect of Aerosol OT and Product QB on the Inhibition of Merthiolate for S. aureus and E. typhosa at Different pH Values***

pH of Agar	5		6		7		8		9	
Organism	S	T	S	T	S	T	S	T	S	T
	Zone of Inhibition (mm.)									
Merthiolate (Aq.)										
1:50,000	4.5	2.0	3.0	1.0	2.0	—	5.2	1.2	5.0	3.0
" and 0.1% QB	4.0	1.2	3.2	0	1.5	0	4.0	0	4.5	1.5
" and 0.1% OT	3.0	1.0	3.5	1.0	2.6	1.5	4.5	1.5	4.5	2.0
Controls										
Water	0	0	0	0	0	0	0	0	0	0
0.1% QB	0	0	0	0	0	0	0	0	0	0
0.1% OT	0	0	0	0	0	0	0	0	0	0

*Merthiolate prepared by dilution Solution of Merthiolate (Lilly) 1:1000 with distilled water.

**Results indicated represent the average of two separate experiments.

TABLE Xa

The Effect of Lipoids on Inhibition of Merthiolate Solution (1:1000) *for S. aureus and E. typhosa at Different pH Values*

pH of Agar	5		6		7		8		9	
Organism	S	T	S	T	S	T	S	T	S	T
	Zone of Inhibition (mm.)									
Merthiolate (Aq.)										
1:1000	9.8	8.5	8.8	4.5	8.8	7.5	7.4	7.8	9.0	4.8
" and Stearic acid*	8.5	7.2	8.2	3.8	7.8	4.4	7.0	3.8	9.0	3.5
" and Sodium taurocholate**	8.5	7.8	8.2	3.6	8.5	3.5	6.5	4.0	8.5	3.2
" and Lecithin*	8.5	5.0	7.8	3.6	7.4	4.0	5.5	3.5	7.0	4.8
Controls										
Lipoids	0	0	0	0	0	0	0	0	0	0
Ether	0	0	0	0	0	0	0	0	0	0

*Stearic acid and Lecithin were made up in anhydrous ether.

**Sodium taurocholate was made up in distilled water.

TABLE XI

*The Effect of Aerosol OT and Product QB on the Inhibition of Bichloride of Mercury for S. aureus and E. typhosa at Different pH Values***

pH of Agar	5		6		7		8		9	
Organism	S	T	S	T	S	T	S	T	S	T
	Zone of Inhibition (mm.)									
$HgCl_2$ (1:10,000)*										
aqueous	4.0	2.8	3.8	2.0	3.2	3.0	2.2	1.5	2.2	1.5
" and 0.1% QB	3.0	2.8	2.4	1.8	2.4	1.8	1.8	1.0	1.2	1.0
" and 0.1% OT	5.0	2.0	2.8	2.6	2.8	2.0	2.0	1.2	1.2	1.0
Controls										
Water	0	0	0	0	0	0	0	0	0	0
0.1% QB	0	0	0	0	0	0	0	0	0	0
0.1% OT	0	0	0	0	0	0	0	0	0	0

*Dilutions made from stock 1:1000 solution of $HgCl_2$, U. S. P.
**Results represent the average of two separate experiments.

TABLE XIa

*The Effect of Lipoids on Inhibition of Bichloride of Mercury for S. aureus and E. typhosa at Different pH Values***

pH of Agar	5		6		7		8		9	
Organism	S	T	S	T	S	T	S	T	S	T
	Zone of Inhibition (mm.)									
$HgCl_2$ (1:10,000)*										
aqueous	4.8	2.4	4.2	2.5	3.0	3.0	3.5	1.6	1.8	1.8
" and Stearic acid†	2.0	2.0	4.0	2.0	3.0	2.5	2.4	1.0	1.5	1.8
" and Sodium taurocholate‡	3.2	2.4	4.2	2.2	3.0	2.2	3.5	1.4	1.6	2.0
" and Lecithin†	3.0	2.0	3.4	2.0	3.0	2.5	2.5	1.2	1.4	1.8
Controls										
Lipoids	0	0	0	0	0	0	0	0	0	0
Ether	0	0	0	0	0	0	0	0	0	0

*Dilutions made from stock 1:1000 solution of $HgCl_2$, U. S. P.
**Results represent the average of two separate experiments.
†Stearic acid and Lecithin made up 1:100 in anhydrous ether.
‡Sodium taurocholate made up 1:1000 in distilled water.

The Inhibitory Effect of Aerosol OT and Product QB on S. aureus and E. typhosa and the Action of Lipoids on This Effect: In

order to examine more closely the effect of anionic and cationic detergents on both Gram-positive and Gram-negative organisms, two strongly inhibiting detergents were chosen to represent the two types and their action on *S. aureus* and *E. typhosa* was observed at different pH values. The effect of the absorption of the various lipoids on discs of filter paper previously impregnated with either an anionic or cationic detergent also was studied. The effect of the various lipoids on both Aerosol OT and Product QB against *S. aureus* at the different pH values of agar medium is shown in Table VIII.

It will be noted from Table VIII that the inhibitory effect of Aerosol OT against *S. aureus* has decreased at pH 5 and 6 and inhibited completely at higher pH values. The action of Product QB, however, appears to have been stimulated somewhat at low pH values and inhibited slightly by higher pH values. It is interesting to note that oleic acid, an unsaturated fatty acid, exerts the most marked inhibiting effect on both anionic and cationic detergents.

The bile salts, sodium ricinoleate and sodium taurocholate, are least effective in their action on the inhibition of *S. aureus* by Aerosol OT and Product QB. Perhaps, the unusually great affinity of these compounds for fatty substances can explain this phenomenon.

A Study of the Action of Lipoids and Detergents on Disinfectants: The action of several commercial disinfectants on *S. aureus* and *E. typhosa* was examined by the technique described above and the relationship of several lipoids and detergents to this action was investigated. No attempt was made to determine the minimum inhibiting concentration of the several disinfectants but rather, to correlate the action of 0.1 per cent. concentrations of Aerosol OT and Product QB on a known inhibiting concentration of the disinfectant.

Three disinfectants were examined in this study. They were:

1. Solution of Merthiolate—Eli Lilly and Co.
2. Tincture of Metaphen—Abbott Laboratories
3. Bichloride of Mercury (Aq.)—U. S. P., 1:1000, assayed

Fresh solutions of the above disinfectants were prepared as needed and no solution was used which was more than six hours old. All dilutions were made in distilled water.

The Effect of Anionic and Cationic Detergents on Disinfectants: The effect of 0.1 per cent. concentrations of anionic and cationic detergents, Product QB and Aerosol OT respectively, on the inhibiting

effect of the various disinfectants also was examined. The results of this study are given in Tables IX, X, and XI. Unfortunately, results of the addition of 0.1 per cent. of either Aerosol OT or Product QB to the several disinfectants were inconsistent. In most of the cases studied, the inhibiting effect of these solutions was not appreciably effected by the addition of either Aerosol OT or Product QB.

The Effect of Lipoids on Disinfectants: The effects of stearic acid, sodium taurocholate and lecithin were studied in their relation to the inhibitory effect of the above disinfectants. It will be seen from Tables IXa, Xa and XIa that the inhibiting effects of all disinfectants studied were decreased to some extent by the addition of the lipoid substances. The gradation of inhibitory effect from the acid to the alkaline range of the several disinfectants also can be noted.

The Effect of Lipoids on Detergent-Disinfectant Mixtures: The addition of various lipoids to detergent-disinfectant mixtures also resulted in decreased inhibition for *S. aureus* and *E. typhosa.* Photographs of plates showing the results of the addition of 1 per cent. stearic acid in ether to discs impregnated with a 1/10,000 dilution of metaphen and also to discs impregnated with 1/10,000 dilution of metaphen containing either 0.1 per cent. of Aerosol OT or Product QB illustrate this effect. It can be seen that the addition of Aerosol OT to a solution of metaphen increases its inhibitory effect both for *S. aureus* and *E. typhosa* only in the acid range. There is little or no change in the neutral range and possibly even decreased inhibition in the alkaline range. The effect of stearic acid tends to decrease the inhibition of metaphen solution for *S. aureus* and *E. typhosa* throughout the entire range of pH. See Plates I, II and III for photographic demonstration of the above results.

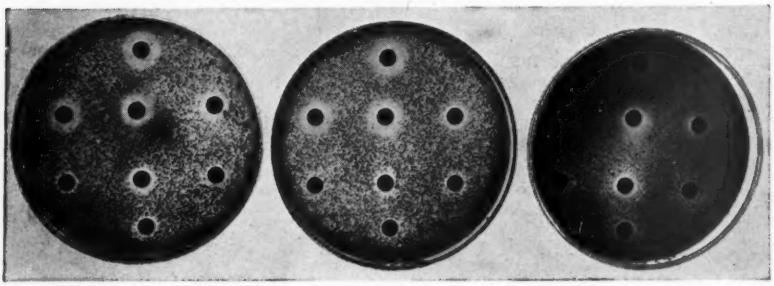
Discussion

The results of the above experiments indicate the important role of lipoids in altering the inhibiting effect of highly active surface-tension depressants and disinfectants on *S. aureus* and *E. typhosa.* The mechanism of this action will be explained in the light of observations made from the above experiments.

The Effect of pH: Anionic detergents have proved most active in the acid range while cationic detergents show greatest activity in the alkaline range. The action of metaphen (1/10,000 Aq.) parallels

PLATE I

Effect of Lipoids on Inhibition of Aerosol OT and Product QB for S. aureus at Different pH Values



pH Agar 5 7 9

A
B C D
E F G
H

A. Aerosol OT 1.0% aqueous.
B. Aerosol OT 1.0% aqueous and 1.0% stearic acid in ether.
C. Aerosol OT 1.0% aqueous and 0.1% sodium taurocholate in water.
D. Aerosol OT 1.0% aqueous and 1.0% lecithin in ether.
E. Product QB 1.0% aqueous and 1.0% stearic acid in ether.
F. Product QB 1.0% aqueous and 0.1% sodium taurocholate in water.
G. Product QB 1.0% aqueous and 1.0% lecithin in ether.
H. Product QB 1.0% aqueous.

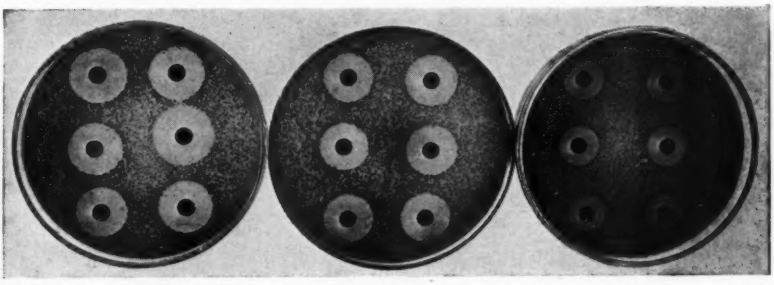
that of anionic detergents with respect to the effect of pH. Note decreasing gradation in inhibition at pH values of 5, 7 and 9 as indicated in Plates II and III.

Gershenfeld and Perlstein (26, 27) have shown the effect of pH on the bactericidal effect of Aerosol OT. Baker *et al.* (4) also have shown that the inhibitory action of both anionic and cationic detergents was markedly influenced by hydrogen ion concentration. Ordal *et al.* (46) reported that the germicidal action of solutions containing buffer, phenol and wetting agents decrease with an increase in alkalinity from pH 9 to 11, although the germicidal action of solutions of buffer and wetting agents increase in the same range.

The effect of hydrogen ion concentration on the inhibition of detergents and disinfectants for *S. aureus* and *E. typhosa* may be due to several factors. Baker *et al.* (4) tend to point out that the forma-

PLATE II

*The Effect of Stearic acid** and Detergents*** on the Inhibition of Metaphen* for S. aureus at Different pH Values*



pH Agar 5 7 9

A B
C D
E F

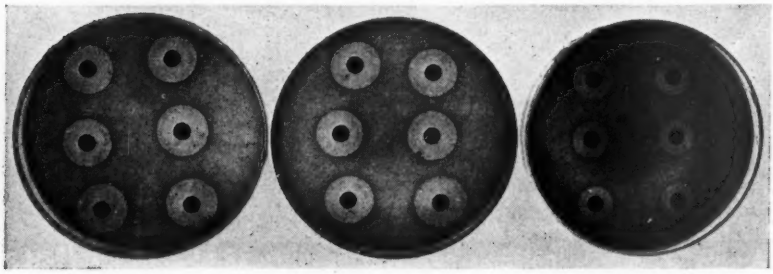
A. Metaphen (1/10,000) plus 1.0% stearic acid.
B. Metaphen " "
C. Metaphen " plus 1.0% stearic acid and 0.1% OT.
D. Metaphen " and 0.1% OT.
E. Metaphen " plus 1.0% stearic acid and 0.1% QB.
F. Metaphen " and 0.1% QB.

*Prepared fresh from Tincture of Metaphen (Abbott) in distilled water.
**Stearic acid, 1/100 diluted in anhydrous ether.
***Detergents: OT = Aerosol OT made up fresh from stock 5% solution.
QB = Product QB made up fresh from stock 5% solution.

tion of undissociated ions make for greater activation, because of greater ability to enter the cell. The pH effect might be due to greater adsorption. Rideal (59) emphasized the importance of pH of the medium in penetration of fatty acids into the protein monomolecular film layers. He further showed the importance of the carboxylic group in anchoring fatty acid molecules and showed that the lipo-protein complex thus formed is forced into solution and dispersed, thus reverting the protein film layer on water into one of fatty acid. This phenomenon might explain the inhibiting action of fatty acids on the bacteriostatic effect of detergents and disinfectants for *S. aureus* and *E. typhosa*. Harkins (34) described the effects of changes of hydrogen-ion concentration upon the thickness of protein

PLATE III

The Effect of Stearic acid and Detergents on the Inhibition of Metaphen for E. typhosa at Different pH Values



pH Agar 5 7 9

A B
C D
E F

A. Metaphen (1/10,000) plus 1.0% stearic acid.
B. Metaphen " "
C. Metaphen " plus 1.0% stearic acid and 0.1% OT.
D. Metaphen " and 0.1% OT.
E. Metaphen " plus 1.0% stearic acid and 0.1% QB.
F. Metaphen " and 0.1% QB.

See footnotes for Plate II.

films. He showed that the thickest films were obtainable at the isoelectric points of the proteins studied with tendency for protein dissolution on the extreme acid and alkaline sides. No doubt the isoelectric point of the bacterial proteins also plays an important role in the phenomenon of the inhibiting action of detergents and disinfectants. The ion effect of the active non-polar portions of anionic and cationic detergents respectively has been shown to govern the essential mechanism of the action of these compounds.

Effect of Surface Tension: Surface tension has long been associated with physiological activity of bacteria. Larson *et al.* (40) in a series of experiments conducted with regard to the growth of different types of bacteria in broth the surface tension of which was conditioned by the addition of surface tension depressants, suggest the importance of lowered surface tension of media to the activity of bacterial growth. Frobisher (24, 25), employing phenol as the germicide,

sodium oleate as a surface tension depressant, and *E. typhosa* as the test organism, showed that within a comparatively narrow range of concentration the presence of sodium oleate with its tendency to reduce the surface tension increases the germicidal efficiency of phenol. Smaller amounts retard the action of the phenol and larger amounts interfered with the ability of the phenol to kill *E. typhosa.* From the above, it would seem that larger amounts of the reducent were sufficient to form a protective film around each bacterial cell and thus prevent close contact of cell and phenol.

The work carried out in this study indicated the lack of any definite correlation between surface tension and bacterial inhibition. All surface tension reducents studied here have approximately the same surface tensions (30-35 dynes/cm.) in a 1 per cent. concentration, yet it has been definitely shown that they vary in their inhibiting effect for *S. aureus* and *E. typhosa.* There is no doubt that chemical configuration and hydrogen-ion concentration might confuse the interpretation of surface tension results with regard to their respective inhibiting effects.

In correlating the surface tension of the various disinfectants studied with the zones of inhibition produced against *S. aureus* and *E. typhosa,* it was found that the addition of either Aerosol OT or Product QB in a concentration of 0.1 per cent. to the various disinfectants reduced their respective surface tension values to approximately the same value (27-32 dynes/cm.), yet their inhibitory effects varied sometimes as much as 100 per cent. In some cases the inhibitory effects of some of the disinfectants studied were actually diminished upon the addition (and consequently lowering of surface tension) of Aerosol OT or Product QB.

Effect of Lipoids on the Action of Detergents and Disinfectants for S. aureus and E. typhosa: It has been shown that lipoids tend to diminish the inhibitory effect of synthetic detergents and disinfectants for *S. aureus* and *E. typhosa.* It also was shown that the effect of an unsaturated fatty acid was greater than that produced by any of the other lipoids. The affinity of the unsaturated group for oleophilic groups in the lipo-protein layer of the membrane covering the bacteria serves to block the action of the detergent or disinfectant. The availability of fatty acid molecules in the phospholipids and sterols studied no doubt explains the fact for their respective display in inhibiting the action of detergents and disinfectants. The complex

structure of these compounds, however, tends to modify their action. By their physico-chemical action, therefore, these lipoids alter the affinity of detergents and disinfectants for bacteria by their direct effect on the cell membrane. Sobotka (50) pointed out that the various bile salts are distinguished by their great affinity for all sorts of fatty substances, hydrocarbons, etc. He further indicated that their unique molecular structure enhanced with numerous methylene groups is responsible for their excellent emulsifying abilities. This will aid us in understanding the minor effect of sodium taurocholate in minimizing the inhibiting effect of detergents and disinfectants for *S. aureus* and *E. typhosa*. He also mentioned the molecules with uninterrupted sequences of methylene groups found in the acids contained in chaulmoogra oil, which appears to be a powerful agent against the bacillus of leprosy, a microorganism with a lipoid envelope.

Baker *et al.* (7) pointed out that the affinity of emulsifying agents to bacterial cells may tend to denature the proteins found in their membranes. Lawrence (59) indicated the dissociating effect of fat-like substances for protein molecules. Rosenbloom (52) in an excellent review of the methods in which lipoids combine with cells has shown the complex nature of lipoid combinations with various inorganic and organic constituents of the cell membrane. Osterhout (59) constructed models of protoplasmic surfaces and was able thus to study the relationship of membrane structure and lipoid affinity.

Summary

1. A technique is presented based on the production of a zone of inhibition when a disc of Whatman No. 2 filter paper, 5.5 mm. in diameter, is impregnated with a detergent or disinfectant, dried for one-half an hour in an incubator at 37.5° C. and then transferred to the surface of a previously inoculated agar plate.

2. A study of the inhibitory effects of anionic and cationic detergents as well as of several commercial disinfectants has been made by means of this technique.

3. The effect of the action of both Aerosol OT and Product QB in concentration of 0.1 per cent., on inhibiting the activity of several disinfectants was noted. The inhibitory action of several lipoids on the effects of detergents and detergent-disinfectant mixtures for *S. aureus* and *E. typhosa* at different pH values also was investigated.

4. The role of hydrogen-ion concentration in the evaluation of wetting agents and disinfectants was shown by this technique and the work of former investigators (26, 27, 29) was confirmed.

5. The nature of the part played by surface tension in this mechanism has been shown to be secondary.

Acknowledgment

Our thanks are extended to Miss Moser of the Department of Pathology of the University of Pennsylvania Medical School for her excellent preparations of the photographs included in this work.

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SCIENTIFIC KNOWLEDGE IS A PUBLIC TRUST

By T. Swann Harding

The opinions expressed here are solely those of the author and not necessarily those of this Journal. Mr. Harding represents that ever-growing group of socially conscious individuals who insist that changes in our ways of doing things must come. Those who disagree will argue that private initiative, essential in a free state, will surely cease if such changes are made. Whichever side you support this article will hold your interest.—Ed.

INVESTIGATION recently disclosed that I. G. Farben of Germany and Standard Oil of New Jersey, used patents as offensive weapons to better their positions and as defensive weapons to resist the efforts of other companies to better theirs. They were playing the great synthetic-rubber game according to the old fashioned rules of international big business. Standard Oil had to build a strong patent structure or else pay heavy tribute to other companies, but in the end the entire Nation paid the bitter costs in unpreparedness before the onslaught of totalitarianism.

These two giant companies divided the world between them and sought to stifle competition. But in the process I.G.F. withheld from Standard Oil valuable "know-how" technical information thus rendering the patents turned over by the former all but useless to the latter. Meanwhile Standard trustingly turned over to the Germans a hundred or more valuable octane-gasoline findings, though it gained essentially nothing at all in return. Patents were used for cartel protection.

Hence plans for large-scale production of general-purpose synthetic rubber were never worked out in this country and the possibilities of technical development were not even fully explored. Such huge royalties were charged for the use of patents which were available that none could afford to pay. That was the intent, for the patents were used merely to consolidate monopoly. As a result we were caught in a moment of dire need without facilities for the production of urgently necessary synthetic rubber.

This is what comes of corporations using patents as weapons to maintain their business positions rather than for public service and the national welfare. Scientific knowledge should not be so prostituted. It is our racial heritage. The law should at least make all inventions given patent protection available on fair terms to all who desire to use them. But how necessary are patents themselves?

On a number of occasions industrialists and businessmen testifying before the Senate Patents Committee have voiced the idea that industrial secrecy and the patent structure are absolutely essential to give incentive for scientific progress. Yet almost exactly the reverse of this proposition is true. For a generation or two past research workers have operated as salaried teams. The old days when an individual inventor struck it rich or was capitalized after his discovery by some one firm have gone long since.

Viewed broadly scientific knowledge is our heritage as a race. The process of scientific discovery is always a gradual one in which many individuals, some living and some dead, have their part. The body of knowledge so accumulated really belongs to our society as a whole and should be held in public trust for the promotion of the public welfare. It belongs to all humanity, for in one way or another everyone helped accumulate it. The question of patents on scientific discovery is, nevertheless, a complex one.

Basically the position of science and of scientists in our society is an anomalous one. Science and intellect cannot be wholly repudiated, of course, even by totalitarian gangster states, but their position has been none too secure in the freest and most democratic nations. Science tends to be skeptical and iconoclastic. It examines all contentions and all institutions dispassionately. It recognizes no sacred preserves and no cleavage between sacred and profane. It intrudes as readily one place as another. It recognizes no external authority as final, hence there must be latent hostility to science in every human society.

True the general run of men accept the fruits of science—the gadgets and the conveniences. But such social support as science has had went to it because it demonstrated power, produced things people desired, and discovered knowledge that could be exploited commercially. On the other hand, since the creator is not the exploiter, the scientist tends to become an object of reproach every time end results of his work evoke the disapproval of pressure groups.

There have been many calls for a breathing spell, a vacation for research, in the past. Many have cried out that technology must take a rest to enable society to catch up with it. The increasing complexity of scientific research has made scientists unintelligible even to one another. The layman finds such scientists remote and esoteric and must take what they say on faith. In general humanity has taken the results of scientific research and produced arrogant millionaires and abject slums, armaments and the desolation of war.

Meanwhile organized research has itself become a major industry. This industry expends something like three hundred million dollars a year and in peacetime employs from seventy to a hundred thousand individuals. It takes at least thirty thousand dollars a year to finance the average research program of a concern with an annual gross income of about a million dollars. Such a firm would employ a scientific staff of about a half dozen. Obviously very small firms cannot afford the luxury of research.

It is also quite obvious that patents and secrecy make a great deal of duplicating research necessary. In the long run there really are no such things as industrial secrets. One industry is compelled to find out what another in a similar line is doing in order to compete on something like even terms. This is done by hiring a scientific staff to discover what the scientists in the competitor's laboratories already know. Patents enable large firms to suppress much knowledge and to keep it in cold storage unused as long as desired.

The whole process of industrial secrecy and patenting is in fundamental opposition to scientific ethics and morality. All scientific discovery is a gradual process and no one individual can ever honestly be cited as wholly responsible for the results. Furthermore the great basic discoveries in the realm of pure science upon which all else builds usually are not patentable. That is generally because they only become susceptible to commercial exploitation after undergoing minor practical transformations which applications are patentable.

In the field of medicine alone there were ten practically simultaneous inventions of the laryngoscope and five independent discoveries of adrenalin. There were eight simultaneous discoveries of the cellular basis of life and five officially recorded demonstrations of the clinical value of cowpox vaccination before Jenner. There were five independent introductions of ether, and the ophthalmoscope was invented simultaneously in Germany and in England.

Work on the insecticide rotenone, and similar substances, proceeded simultaneously in Germany, England, Japan, and the United States. The discovery that liver therapy was effective in anemia had been made in Italy many years before Whipple, Minot, and Murphy made it again. The laws of genetic inheritance were re-discovered simultaneously in England and the United States, though Mendel had originally discovered them fifty years earlier. The preparation and use of extracts from the pancreas which contained insulin was announced many years before Banting and Best rediscovered, perfected, patented, and controlled the process.

Hundreds of other examples could be cited. Obviously there is something basically unfair about granting either prizes or patents to the individual who finally puts a discovery over the top. There was nothing new in Darwin's evolution theory, for instance; he merely very methodically adduced the evidence for it. But he put evolution over. Yet he also built upon the work of other men, many of them long since dead.

Patents are ethically unfair because they give undue credit to the person who makes the last push over the top. A while ago certain Wisconsin workers patented a method of producing vitamin D by irradiating certain organic chemicals. Priority was immediately contested by another worker in this country and, it seems, with warrant, while the patent also ignored indispensable work by British and other foreign investigators.

At times commercial firms form valuable alliances with academic institutions by establishing fellowships which they support in whole or in part. Thereafter they claim and horde or exploit the knowledge produced, whichever best serves their purpose. They also take the poorly paid scientists who made the rich finds into their own laboratories if that seems expedient.

The more truly an individual is a scientist the more easily he can be exploited at low pay, because he does research really for the fun of it. His major reward is the feeling of satisfaction or elation that results from having added another driblet to humanity's store of scientific knowledge. His results should enrich society as a whole for this very reason.

Most scientists are neither avaricious nor acquisitive. They feel like they are getting paid for what they love to do anyway. They are therefore easily exploited, while they tend to disregard the use ulti-

mately made of their discoveries as a matter which does not concern them. In that sense they serve society ill.

Originally, of course, research was the hobby of independently wealthy amateurs who felt no social or other obligation to publish what they had discovered. They often kept their notebooks in a strange rubric none could decipher but themselves. Yet so long as such secrecy ruled, scientific progress was slow and halting. In any case the question of property rights in a scientific discovery does not tend to arise until commercial applications become possible.

When that point is reached the discovery will nearly always be found to have resulted from the successive researches of many scientists in many lands. Much new knowledge may remain for years in the domain of pure science, but even it is drawn upon from time to time, in the making of further discoveries many of which lead to profitable commercial applications. Patent law ill applies to this field anyway. The production of highly potent vitamin D by ultraviolet irradiation of certain complex substances, as observed above, was based upon fundamental and unpatented discoveries of many workers.

That is generally true of research findings. Yet one university patented this and subsidiary processes covering milk and other foods. It made admirable use of the revenue from the patents it is true, and as early as 1931 the royalties were coming in at a rate of a thousand dollars a day. But what of the social utility of the patents—say the one on vitamin-D milk?

Some manufacturers held there should be no difference in the resale price schedule between irradiated and unirradiated milk. But others held that this would merely result in monopoly control of such milk by five or six companies which had exclusive licenses for the process. They contended that unless the irradiated product sold higher, though it really cost little more to make, brand names could not be used effectively to exploit it—i. e. to make the public pay quite a great deal more for it.

Moreover, extensive advertising of the irradiated-milk process would be prejudicial to firms using cod-liver oil as a source of vitamin D. However, the university contended it must limit the licenses it issued to a small group of firms which were engaged already in an expensive campaign of national advertising. But it frowned on the use of vitamin D in chewing gum and frankfurters, though these advertised widely. Of course it is harder to sell vitamin-D milk if the vitamin can also be purchased in gum and hot dogs.

The license system was prejudicial to certain producers also who had to be denied its use. Limitation of the licenses to the half dozen companies that controlled 60 to 65 per cent. of the Nation's evaporated milk business perpetuated and enhanced monopoly. This added great strength to already powerful companies which needed it least. Certain effective competitors, like the chain-store organizations, appeared to be effectively excluded.

The license as granted by the university foundation thus really gave monopolists another weapon for maintaining their advantage over their competitors. Nor could the foundation do anything to protect consumers from excessive prices. Yet, unless the number of licenses granted was limited, their value was lost and royalties would not flow to the university. Obviously then the companies able to pay most for the licenses were in a position best to exploit them. The long and short of it is that this method of patent control does not result in maximum social advantage.

After all, this particular application of vitamin D is a minor scientific finding anyway. Perhaps the individual who deserved the patent and the reward was the one who first demonstrated that such things as accessory food elements or vitamins existed. But that person received no patent; furthermore he also built upon the work of earlier investigators.

The greatest scientists did that. On October 6, 1807, Humphry Davy made tiny globules of molten potassium which broke through the water and took fire when he passed an electric current through fused caustic potash. That was a great major discovery, but Davy got no patent on it. Furthermore he built on the observtion of Nicholson and Carlisle, April 30, 1800, that water could be decomposed by the voltaic pile or electric current—a purely accidental observation.

Davy's discovery became the basis for all our great electrolytic industries—for getting caustic soda from common salt to make soap, for instance. Many years later Charles Martin Hall of this country used the same idea to make aluminum from bauxite which readily dissolves in aluminum fluoride or cryolite, forming a good conductor.

Take another instance. In 1820 Oersted, a Danish physicist, observed that if a compass was suspended near a wire carrying an electric current, the needle was deflected. Davy next reasoned that there should be a tendency when the pole of a magnet was presented towards such a wire, for the wire to turn or twist on its own axis.

Then Farraday showed that a wire carrying an electric current would rotate around a maget over which it was suspended. The principle of the electric motor was thus evolved without secrecy, without patents.

Men like Couper, Kekule, Pasteur, Arrehenius, Van't Hoff, Newlands, and Mendelejeff worked out the entire basic architecture of modern chemistry. They enabled chemists to find their way through the forbidding mazes of organic compounds. Business and industry later built on this work. Clerk Maxwell and Heinrich Hertz worked out the fundamental principles of electrical science often later attributed to those famous pickers of the brains of others, Marconi and Edison. Marconi or somebody like him was simply inevitable after Maxwell.

Catalysis was discovered by the pure intellectual work of numerous scientists and now performs industrial miracles. Photo-electric effects underlying modern sound effects for movies and television were based on fundamental discoveries by Hertz in 1887 and Hallwachs in 1888. Investigation of the electrochemical equivalents of metals and alloys yielded data making modern canned foods possible, and Gibbs' phase rule made possible modern alloys and underlies much of our metallurgy.

Priestley, the heretical parson who discovered oxygen, certainly never thought of the oxyacetylene blowpipe or of therapeutic uses of oxygen gas, but these came about in time. The investigation of rare inert gases in the atmosphere in minute quantities brought us heavier-than-air navigation, electric signs, neon lights, tungsten electric bulbs, mixtures of helium and oxygen for use in asthma and caisson disease, and so on. Obviously the basic workers were sparsely rewarded save in the intangible coin of intellectual satisfaction.

When a scientist makes and confirms a finding the next necessary step is to publish as freely as he wishes. Only by such widespread and continuous free communication between scientific workers the world over can science progress. Industrial secrecy and the patent system directly block such progress. They tend also to the suppression of knowledge which could be of great social value. No scientist can really rest content when his discovery is thus pigeonholed and he is remanded to his laboratory to discover something else which may in its turn be suppressed.

Bernhard J. Stern tells of 3,400 patents suppressed by the Bell Telephone Co. alone of which 1,307 were said to have been shelved voluntarily by agreement between the company and the patent holder. Public convenience was secondary here, the primary motive having been to forestall competition. Yet, Stern says, only 12 of the 75 basic inventions made between 1889 and 1929 resulted from corporation research; the rest resulted from academic or government research.

At the same time because the carrying on of research is an expensive affair, only the larger concerns can afford it and research thus becomes integrally associated with monopoly. It takes at least $75,000 a year to operate a laboratory staffed by a score of workers. In such teamed groups the field of research is carefully controlled and the timing as well. If it appears that it will not pay to introduce practical applications of research at a certain time the knowledge is suppressed until prospects of profit are more favorable. The continued security and profitability of the industry is paramount.

In this process scores of protective patents are filed but never used. Much time is devoted to finding out what the other fellow already knows. Valuable pools of scientific knowledge are accumulated and held as a personal possession. The advantages of large over small concerns are constantly widened.

An example of the boondoggling to which research workers are reduced because of patent and secrecy policies is the various special mercuric dusts for the control of rusts, stripes, and smuts in cereals. Work began originally in Germany. Ultimately very effective dusts could be made very cheaply, but the compositions and processes were secret. After 1925 huge combines began to control these dusts as they did many other commodities. Science and plant pathology suffered.

By this time the ablest research men worked for the largest and richest concerns. They refused to divulge their findings in full or, if they did in part, you couldn't tell where truth ended and propaganda began. By 1934 government scientists had to waste an extraordinary amount of time not seeking new knowledge but re-discovering that which had been withheld deliberately for price maintenance. Their task was doubly difficult because they lacked the laboratory resources of the great chemical works, but finally they succeeded.

The same sordid story may be told regarding other products. In general scientists on salaries aided inefficient and uneconomical industrial concerns to derange the entire system of production and con-

sumption and to sabotage technology because of the commercial need for price maintenance. Incredibly uneconomical use was made of natural resources and an extravagantly wasteful organization of equipment and manpower was effected even in highly mechanized industries.

As in the case of the mercuric dusts, academic and especially State and Federal Government research has been the main bulwark of the public. In recent years the Federal Government has expended around a hundred and twenty-five million dollars annually on research. The range of such research is wide, the field of agriculture being one of the most notable. A single bureau of the Department of Agriculture estimates that accomplishments of its scientists bring to agriculture and industry an increased income of a quarter of a billion dollars a year.

Government research has also done much to stimulate outside research; at other times it has protected consumers from exploitation, both by finding the formulas of, or satisfactory substitutes for, high-priced patented or trade-marked products, or by analyzing frauds and denying them the market. Secrecy does not exist here. If any patents are procured they are public-service patents which turn the knowledge loose for any who wish to make use of it. The accomplishments of such research indicate that secrecy and private patents are not necessary incentives for the achievement of progress.

Government research findings now save the southern yellow pine industry ten millions a year formerly lost by the de-grading of lumber which was improperly kiln-dried. They have added ten or fifteen millions a year to the income of milk producers by increasing milk butterfat content and, by developing better methods of butter making, have added at least five millions a year to the income of the butter industry.

If only 5 per cent. of the projects undertaken yield practical results, even then the returns on such research run from 500 to 10,000 per cent. But while Government research has enormously aided the farmer in the general technology of crop production he faces patents, secrecy, monopoly, and exploitation when it comes to purchasing such things as insecticides, fungicides, fertilizers, and agricultural machinery.

In 1940 the Federal Trade Commission announced its finding that nine agricultural machinery and tractor manufacturing corpo-

rations sold nearly ninety-four per cent. of all products in this field. Actually two firms dominate the industry, and four have effective control of its output. Yet agricultural machinery was developed by technically trained and scientifically minded inventors who, however, were secretive about their work and resorted to patent protection.

Several things become apparent from this brief review. One is that scientists and scientific institutions, wherever located and regardless of the kind of work in which they are engaged, should at all times have absolutely free intercourse with one another. There should be no restraints whatever imposed upon scientific workers other than those which constrain all citizens of a democracy. Science also requires better organization, better means of evaluating its own state at any particular time, more methodical methods of filling gaps in knowledge so that all the sciences may advance on an even front.

In view of the staggering returns scientific research has paid both to private industry and in the form of social dividends, it is ironical indeed that it has habitually been short of sufficient funds for full support. In wartime especially we depend upon science and technology for our very salvation and even the totalitarian nations with their natural contempt for the scientific method and spirit yet call upon science for indispensable aid. Certainly nations which can so freely spend billions for warfare should have a few more millions for the generous support of pure research after hostilities cease.

Once more, as was said in the beginning, scientific knowledge is our racial heritage. It belongs to all of us as a people. In one way or another we have paid for it. If it was carried on by Government agencies we paid for the basic research in the form of taxes; if it was carried on by private enterprise we as surely paid for it in the form of an increase, however slight, in the price of the goods and equipment we buy. The charge forms part of the firm's "overhead."

Because scientific knowledge is the product of many minds and because research is in last analysis supported by the public at large, such information should be so utilized as consistently to enrich human culture and promote human welfare. Therefore it should be held in public trust and no private enterprise should ever be permitted to maintain some of it secret in order to exploit it commercially regardless of social consequences.

Scientific discoveries should all be covered by public service patents just as such discoveries made in government institutions are at

present. Licenses under commercially usable patents should be granted to manufacturers nominated after careful investigation by a duly qualified board of experts. These manufacturers should have high records for honesty, efficiency, integrity, and true public service. Moderate royalties only would be charged, but these would be ample to support research generously. Scientists would no longer have to go hat in hand to beg for their very existence every so often.

Naturally this system would not wipe out all injustice at once but it would be a long step in the right direction. For instance the granting even of public patents tends to give too much credit to the last workers who pushed the thing over the top. But that would seem less bad when the patent was dedicated to the public and did not become the property of a private enterprise which might at will suppress it or use it to exploit the public commercially.

Large concerns would also still tend to profit most from the use of scientific knowledge. But that brings up another problem, the problem of compelling great monopolies actually to become efficient and to turn them in reality into the public service institutions they now so often merely pretend to be for advertising purposes. Undoubtedly a great deal more of that will be done after hostilities cease.

For, like depression, war has shown that the system of private enterprise is incapable of functioning efficiently in an emergency. Democratic dictatorship and regimentation must be used to enable industry to cope with wartime problems. Every past war has increased government interference in business for obvious reasons and this interference has never been relaxed entirely after the war ended.

Meanwhile, right during the war, we should accustom ourselves to the idea that scientific knowledge is a public trust and must be so regarded at all times. Only by the intelligent control and utilization of scientific knowledge after this war ends can we hope to mainain international peace and improve the living standard of all people. In this free world of tomorrow it is hoped that we may come into the material abundance science and technology made it physically possible for us to enjoy a generation ago but which we have so far spurned.

THE GOVERNMENT NEEDS QUININE AT ONCE!

Contribute All You Can Spare Through the Philadelphia College of Pharmacy and Science

Quinine, quinidine, cinchonine, cinchonidine, and their salts, are necessary for the protection of our armed forces in the Pacific and elsewhere.

Temporarily the supply of these alkaloids has been tremendously curtailed, and the established quota for each man in our armed forces is given as four ounces per year.

Accordingly, you will see that the need is urgent. You will see also how in supplying your contribution of these important medicinals you will be truly helping the war effort.

Reading this authentic and pathetic item from the diary of a war nurse reporting the epic of Bataan:

> "We were running low on everything except the invaluable sulfa drugs and anesthetics. OUR QUININE WAS ALMOST GONE, AND BEFORE we left Bataan, 85 percent of our nurses had had malaria."

Now, this is the plan:

The War Production Board has gladly accepted an offer from the Philadelphia College of Pharmacy and Science to collect, except in the Southern States, all donations of rarely used cinchona alkaloid salts, or, indeed, of any surplus stock of this material which the pharmacist may be willing to contribute without charge to the Government. This College will undertake to identify, pool, and assay all materials received, without charge, and certify them to the Defense Supplies Corporation of the Government. The pooled material will not doubt be converted into quinine sulphate or hydrochloride.

Domestic use of quinine and similar substances can be and has been greatly reduced except in the treatment of malaria. The use of quinine in hair tonics is now a crime, and other materials can replace it in the doctor's prescription for colds, etc. Accordingly, pharmacists may return surplus stock of unopened packages for credit to their wholesalers, or else they may participate in the plan noted above.

Will you, therefore, accept this challenge? Send to the Philadelphia College of Pharmacy and Science any old opened packages, or portions of such, containing any salt or compound of quinine, quinidine, cinchonine, cinchonidine. Your contribution will be recorded and the College will proceed to pool and analyze these stocks. What a fine tribute will accrue to pharmacists the country over if a substantial contribution of these urgent medical necessities can be made at this time. Will you do what you can now? The need is great!

Let there never be another occasion when lack of quinine to fight the dread malarial diseases will further handicap our gallant soldiers and sailors out on the far-flung tropical fronts. Every ounce counts! Quinine is ammunition! Please send your contribution to the war effort now!

Address your package:

QUININE POOL

Philadelphia College of Pharmacy & Science
43rd St., Woodland and Kingsessing Aves.
Philadelphia, Penna.

The War Production Board Has Made the Following Urgent Notice to All Pharmacists Regarding the Tube Salvage Campaign

If the tin salvage program is not successful, it is possible that metal tubes will not be available for packaging.

Large quantities of tubes are accumulating in the hands of retailers, churches, Boy Scout, Red Cross, and other organizations. In many cases they are being held under the mistaken belief that they will be paid for the tubes. The law, however, specifically states that tubes cannot be bought or sold.

There seems to be considerable confusion about the method of collecting tubes. The directions for retailers are as follows:

1. Retailers having stores within the truck delivery zones of their wholesalers are requested by the War Production Board to turn their collections over to the wholesaler's truck at least once each week.

2. Retailers having stores outside of the truck delivery zones of their wholesalers are requested, as soon as they have five pounds or more of empty tubes, to pack same securely and ship by parcel post or express collect to the nearest wholesaler, or to Tin Salvage Institute. The wholesaler will refund postage or pay express charges and will be reimbursed by Tin Salvage Institute. Retailers who have collected 100 pounds or more would help matters considerably by shipping them direct to the Tin Salvage Institute, freight collect.

Send tubes to:

TIN SALVAGE INSTITUTE
411 Wilson Avenue
Hillside, New Jersey

ANNUAL REPORT ON THE UNITED STATES PHARMACOPŒIA TO THE AMERICAN PHARMACEUTICAL ASSOCIATION

By E. Fullerton Cook

Chairman of the Committee of Revision

I HAVE the honor of presenting to the members of the A. Ph. A. Convention the first bound copy of the new U. S. Pharmacopœia, Twelfth Revision. Printed sheets of the U.S.P. XII have been sent to all members of the U.S.P. Board of Trustees and Committee of Revision, but the book before you is the first bound copy issued. In a few days, however, other copies will be available to the many who have been anxiously awaiting its appearance, those who will employ it immediately as the basis for medical standards. Those now interested in the U.S.P. not only include the physicians and pharmacists of the United States, but also a number of persons in other countries where our Pharmacopœia has been adopted as the official standard.

The U.S.P. XII will speak for itself, but some of the new and progressive features may properly be called to your attention.

A Five-year Revision, a Bound Supplement in two and a half years, and other Interim Revision Supplements as needed—The U.S.P. XII is the first of the quinquennial revisions and the first to be followed by a "bound Supplement" to appear midway between revisions. The new Pharmacopœia carries an order blank for this bound Supplement, which is to be supplied to each owner of a Pharmacopœia, without additional payment. The order should not be mailed, however, until the Supplement is announced, which is expected to be in December, 1945, approximately two and a half years from this date.

In the meanwhile the Pharmacopœia will continue the practice of issuing "sheet Supplements" whenever these are found necessary to meet emergency needs. These "sheet Supplements" will ultimately be reprinted in the "bound Supplement".

It should be noted that hereafter the title of emergency revisions and additions, heretofore called "Interim Revision Announcements" will now be called "Supplements", and they will be numbered in sequence, as "First U.S.P. XII Supplement", "Second U.S.P. XII

Supplement", etc. The "First U.S.P. XII Supplement" will be pasted inside the cover of the Pharmacopœia when it is sold and will authorize the continuance of certain modifications in U.S.P. standards during the war period, such as the omission of Oil of Lavender from Aromatic Spirit of Ammonia and a temporary rescinding of the packaging requirements for Ergot, etc. This "First Supplement" will also carry several corrections in monographs.

A "Second U.S.P. XII Supplement" is also in course of preparation and will be released at the earliest possible date. This Second Supplement will add a number of drugs carrying the sulfonamide group, also a number of monographs carrying vitamins and their preparations belonging to the Vitamin B group, also an 8 per cent. Solution of Hydrogen Peroxide, Quebracho Extract (to supply tannins for burn dressings), and other substances which are pharmaceutical necessities. These are all supplied at the request of the Army and the Navy to serve as "war medicines". These are equally important, however, in general medical practice and indicate the rapidity of expansion in medical knowledge.

Fortunately the new, continuous revision program of the Pharmacopœia has enabled it to meet every medical need of our military forces and also adjust established formulas and standards to conform to changed conditions brought about by the war.

Additions to the U.S.P. XII—In the U.S.P. XII proper an unprecedented number of new items and preparations have been added, a total of 174, of which 17 came in by Supplements to the U. S. P. XI.*

In completing this new revision of our national Pharmacopoeia in record time, by its established democratic process, too great praise cannot be given the many able, loyal, and unselfish workers who contributed freely of their knowledge and time, often at great personal sacrifice. The remarkable degree of unanimity of purpose between all professional groups in the fields of medicine and pharmacy, and the splendid co-operation of the officials of the Food and Drug Administration and of the National Institute of Health furnish our government with an effective and strikingly representative book of medical standards, as an essential factor in the maintenance of the health of our nation.

*See *A. J. Ph.*, 1942, June, page 205.

SOLID EXTRACTS

Science Briefs for Easy, Interesting Reading

One of the casualties of the war is the American banana. Most people can shrug it off as an inconvenience, but a lack of the fruit is a severe blow to celiac sufferers. This disease, peculiar chiefly to infants and children, prevents the intestinal tract from digesting sugars and starch. Bananas, however, furnish carbohydrates in a form that victims of this disease can assimilate, hence their desirability.

It has been suggested that dried bananas be flown north from the tropics, while other experts have suggested, and are using, strained apples, apricots and pears to supply the much needed dietary factor.

AJP

The Red Cross has placed a challenge before every "red blooded American" in announcing a requirement of 2,500,000 pints of blood during the next year, to be processed into dried plasma and serum albumin for use in war zones and for disasters at home; 50,000 blood donors weekly will be needed to meet this quota.

AJP

Classification and summarization of possible war gases has been made by the Office of Civilian Defense, as follows: vesicants (mustard, lewisite, ethyldichlorarsine); lung irritants (chlorine, chlorpicrin, diphosgene, phosgene); lacrimators (chloracetophenone); sternutators (adamsite, diphenylchlorarsine). Decontamination methods to use against these insidious war agents are among science's beneficial contributions in a time when it seems that everybody has resolved to torture and annihilate everybody else as quickly and as painfully as possible.

Through the courtesy of one of the leading oil refineries in this country we learn that we can make all the synthetic rubber we need from petroleum, if sufficient steel and other vital materials can be diverted from other channels to build new plants. Already, petroleum, in addition to its well known uses, is aiding in the war effort by supplying 100-octane gas for airplane propulsion, petroleum alcohol for explosives, rust preventives to keep our vital machinery in good running condition, special lubricating oil that flows smoothly in extreme hot or cold temperatures, a special grease to enable deadly torpedo propellors to spin properly under many adverse conditions, airplane pulley oils of special nature, a wool fiber lubricant, a stratosphere grease that functions at 13 miles above the surface of the earth, and, finally, an insecticide that prevents all of the insect torture to which many of our soldiers were subjected during World War I.

AJP

The shortage of tung oil has threatened the supply of fast drying paints but research has developed oils reputedly as efficient as tung oil using soybean and linseed oil as the starting point and imparting to them quick, hard drying qualities.

AJP

The present war has undoubtedly increased the tension of our lives and many are those who put in sleepless nights as a result of overwork, worry and strain. Too much war news, in itself, may so upset our thinking and mental equilibrium that there is a serious threat to our health. One should avoid sedatives in such cases and seek some outlet for nervous energy preferably physical exercise. There is an old saying that "health flies in through the muscles and out through the nerves." Sedatives offer but temporary relief at best and continued use ofttimes causes an exaggeration of the very symptoms such as fatigue and irritability for which relief was sought.

BOOK REVIEWS

Two New Volumes Are Brought to Your Attention

Detailing by Druggists. By Tom Jones. 52 pages. Romaine Pierson Publishers, Inc., New York. Price 75c.

This little brochure is indeed worth the reading by every pharmacist who is interested in the greater cooperation of medicine and pharmacy. It is realistic in its treatment in that it points out some of the serious affronts to physicians attributable to pharmacists and how they should be corrected.

Tom Jones reflects the views of this reviewer in showing that pharmacists who want more prescription and professional business must 1. stop selling questionable merchandise and counter-prescribing; 2. approach the physician with sound illustrations of how they may render real service.

Although brief, this little dissertation is indeed a nugget of wisdom easily understood and worthy of attention.

L. F. TICE.

The Dynamic State of Body Constituents. By Rudolf Schoenheimer, late Associate Professor of Biological Chemistry, Columbia University. Harvard University Monograph in Medicine and Public Health No. 3, 78 pages. Harvard University Press, Cambridge, Mass. Price: $1.75.

This monograph is a collection of three lectures prepared by the late Dr. Schoenheimer just prior to his death and delivered at the Harvard Medical School in October 1941 by Dr. Hans T. Clarke of Columbia University.

The concept of the behavior of the human or animal body has undergone a series of changes. The alchemists considered it an example of a perpetual motion machine and its secret was assiduously sought. The work of Lavoisier on combustion altered this concept

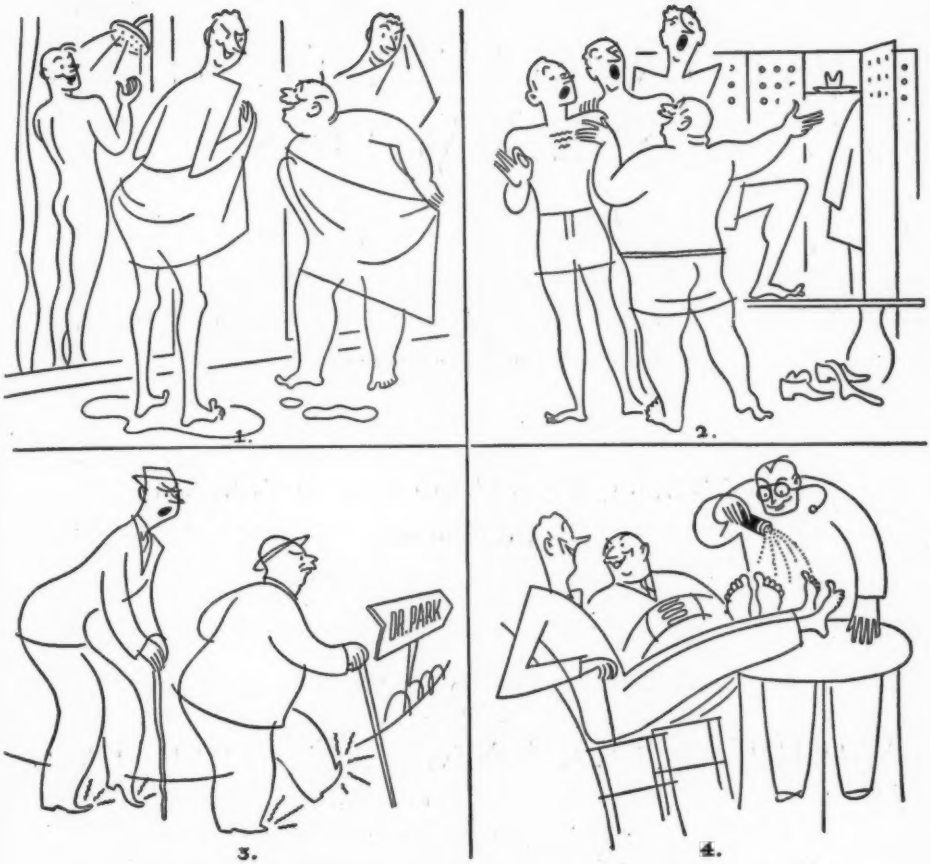
and again and again was the behavior of living tissue restudied upon the introduction of thermodynamics into the picture by Helmholtz and later by the theory of independent exogenous and endogenous types of metabolism. It was not until the work of Urey that any method was available to study the complexity of metabolism. With the development of heavy hydrogen a means was now at hand to form isotopes and since a molecule containing such an isotope is biologically identical with a normal molecule the exact change and fate of the isotope containing substance can be followed.

With this tool at hand a large number of investigations have been carried out and this monograph discusses some of the most outstanding ones and the conclusions that may be drawn. The body constituents are indeed not in any sense static but in a rapid state of flux. Ester, peptide and other linkages open; the fragments thereby liberated merge with others derived from other large molecules and with those absorbed from the intestinal tract to form a metabolic pool of components indistinguishable as to origin. These liberated molecules are again subject to numerous processes with chemical reactions of almost every kind rapidly taking place although so delicately balanced that the body components remain constant in total amount and structure.

Thus the old concept of the body as a combustion engine must be changed to a new one where not only the fuel but the structural materials are in a steady state of rapid flux but yet in thermodynamic balance.

The forces responsible for this arrangement and rearrangement of atoms in biochemical molecules in living organisms is as yet beyond the scope of laboratory study.

L. F. Tice.



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